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Systematic Review

# Does locally relevant, real-time infection epidemiological data improve clinician management and antimicrobial prescribing in primary care? A systematic review

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## Abstract

**Purpose.** Antimicrobial resistance is a significant threat to public health. Diagnostic uncertainty is a key driver of antimicrobial prescribing. We sought to determine whether locally relevant, real-time syndromic or microbiological infection epidemiology can improve prescribing by reducing diagnostic uncertainty.

**Methods.** Eligible studies investigated effects on primary care prescribing for common infections in Organisation For Economic Co-Operation And Development countries. We searched Medline, Embase, Cumulative index to nursing and allied health literature, Web of Science, grey literature sources, thesis databases and trial registries.

**Results.** We identified 9548 reports, of which 17 were eligible, reporting 12 studies, of which 3 reported relevant outcomes. The first (observational) showed antibacterial prescribing for upper respiratory infections reduced from 26.4% to 8.6% ($P = 0.01$). The second (observational) showed antibacterial prescribing reduced during influenza pandemic compared with seasonal influenza periods [odds ratio (OR) 0.72 (95% CI, 0.68 to 0.77), $P < 0.001$], while antiviral prescribing increased [OR 6.43 (95% CI, 5.02 to 8.25), $P < 0.001$]. The likelihood of prescribing also decreased as the number of infection cases a physician saw increased in the previous week [OR 0.57 (95% CI, 0.51 to 0.63), $P < 0.001$ for ≥12 versus ≤1 patient). The third (randomized-controlled trial) showed an absolute reduction in antibacterial prescribing of 5.1% during a period of moderate influenza activity ($P < 0.05$). We did not find measures of diagnostic certainty, harms or costs.

**Conclusion.** There is promising evidence that epidemiological syndromic and microbiological data can reduce primary care antimicrobial prescribing. Future research should use randomized designs of behaviourally informed interventions, investigate costs and harms, and establish mechanisms of behaviour change.

**PROSPERO registration.** CRD42016038871.

**Key words:** Antibacterial agents, general practice, infection, population surveillance, primary health care, public health surveillance.

## Introduction

(i) Antimicrobial resistance is a serious international health threat;
(ii) Diagnostic uncertainty is a key driver of antimicrobial prescribing for common infections in primary care;
(iii) Our systematic review found two observational and one experimental study, showing that real-time, locally relevant, syndromic and microbiological epidemiological data can reduce antibacterial prescribing and
(iv) Future research should use randomized designs of behaviourally informed interventions, investigate costs and harms, and establish mechanisms of behaviour change.

Antimicrobial resistance (AMR) has been described as one of the greatest challenges to modern day public health (1). The over and misuse of antimicrobials are recognized as drivers of AMR, with high levels of poorly targeted antimicrobials are prescribed in the community and 74% of all antibacterial prescribing occurring in general practice (2). The routine use of antibacterials in primary care has been shown to be directly linked to AMR (3,4), and the majority of patients presenting to primary care with an uncomplicated respiratory tract infection in the UK still receive an antibacterial prescription (5).

Clinician uncertainty has been identified as a driver for prescribing antimicrobials in primary care and, therefore, a potential target for interventions looking to affect behaviour change of clinicians (6,7). Furthermore, consideration is required to determine how interventions can address this uncertainty, ensure continued safe management and appropriate prescribing of antimicrobials in situations where they are still required. Horwood *et al*. (8) suggest that additional support is needed for clinicians in their decision-making and interventions that seek to tackle this uncertainty in order to change clinician behaviour are more likely to affect a measurable change.

Improving antibacterial prescribing and reducing AMR are complex problems, requiring complex, multifaceted solutions. This systematic review evaluates one element of what could be a multifaceted approach to reduce clinician uncertainty, improve diagnostic accuracy and reduce antibacterial prescribing. We sought to determine whether locally relevant, real-time syndromic or microbiological infection epidemiology could reduce diagnostic uncertainty and improve antibacterial prescribing. We also sought to describe the theoretical framework of sources contributing to surveillance systems and describe their breadth, purpose, data sources and intended recipients.

## Methods

The review protocol was written following preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (9) and registered with PROSPERO (No.: CRD42016038871).

### Search strategy

The search strategy (Supplementary Table S1) was designed to identify studies investigating the effect on primary care clinician management of common infections in Organisation for Economic Co-operation and Development (OECD) member countries (10) where the intervention includes dissemination of real-time, population-based data on locally relevant microbes or syndromic presentations.

Databases searched were Medline, Embase, Cumulative index to nursing and allied health literature (CINAHL) and Web of Science from database inception to April 2016. Medical subject headings (MeSH) terms and text word searches were combined to produce a comprehensive search strategy covering the following four key areas: 'common infection', 'primary care', 'population-based surveillance' and 'dissemination of information'. Grey literature sources including WHO website and dissertation and thesis registries, including Ethos and Proquest, were searched. Trial registries were also searched including US trial registry (clinicaltrials.gov), European Union (EU) clinical trial registry, International Standard Registered Clinical/Social Study Number (ISRCTN) register and meta-register of controlled trials and the health research authority (HRA) register. Searches were conducted for records in any language. Full-text papers were subject to citation searches.

### Study selection

Eligible studies were those investigating effects on primary care clinician management of common (respiratory, gastrointestinal, urinary and skin) infections in OECD member countries where the intervention included dissemination of real-time, population-based data on locally relevant microbes or syndromic presentations. Eligibility was assessed based on a hierarchy of factors: first, records were initially assessed for meeting the criteria of a common infection, and surveillance systems for conditions such as human immunodeficiency virus (HIV), tuberculosis and malaria were excluded (see Supplementary Table S2 for examples of excluded conditions); second, they were checked for being conducted in an OECD member country; third, studies were assessed for being conducted in a primary care setting and finally that they disseminated information to primary care clinicians, which was locally relevant (provision of data to clinicians more specific than national-level data) and in real time (provision of data to clinicians at least quarterly or more frequently).

One reviewer (IL) undertook initial title screening. At the next stage, the title and abstract screen was undertaken by one reviewer (IL) with a random 10% sample checked by a second reviewer (AB). A kappa statistic of 0.69 demonstrated substantial agreement between reviewers (11). Full-text records were assessed by two reviewers (IL and AB), and any disagreements resolved by discussion or, if needed, consultation with a third reviewer (ADH).

### Data extraction and quality assessment

The following data were double extracted by two reviewers using a purpose-designed spreadsheet: author; year of publication; journal, study design; study country; OECD status; study setting; recruitment and details of participants; description of intervention; source and scope of surveillance data; mode and frequency of intervention dissemination; use of comparator group. Primary outcomes of interest to the review were antibacterial prescribing rates, secondary care referral rates and any harms attributable to the intervention. The secondary outcomes were types of antimicrobials or adherence to guidelines, consultation rates, costs and clinician diagnostic certainty.

We used the Cochrane Risk of Bias (ROB) tool 2.0 (12) to assess the quality of studies using a randomized controlled trial methodology, and we used the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool to assess study quality for non-randomized intervention studies (13).

### Data synthesis and analysis

Through familiarization with the literature during the screening process, we planned to better understand and summarize the range of surveillance systems in use to be able to describe existing surveillance systems within the scope of this review. We conducted a narrative synthesis of the eligible studies and planned to conduct a meta-analysis if appropriate.

## Results

We identified 9548 records through database and additional searches (Fig. 1). Of these, 1693 were duplicates, 4018 were excluded on the basis of the title and 3799 were excluded following second title and abstract screen leaving 38 records to be retrieved in full text from the database and additional searches. A further 10 records were identified from reference lists, and an additional 2 records identified through contacting experts. We obtained these 50 records in full text; of which, 33 did not meet our eligibility criteria. Of these 33 records, 5 were regarding conditions not considered common infections in primary care, 3 were not within OECD countries, 10 were not in a primary care setting, 11 did not disseminate any information and 4 were not locally relevant. Of the 17 records eligible for inclusion, several records report on the same study leaving 12 eligible studies for inclusion (14–25) with the remaining 5 records providing supporting material (26–30).

Of the 12 eligible studies, the principle records for each study included 10 publications in peer-reviewed journals (14–21,23,24) and two conferences proceedings (22,25).

### Surveillance systems

Figure 2 shows the wide variety of surveillance system purposes (including AMR, surveillance, bioterrorism and food safety, as well as infection surveillance), data sources and intended recipients.

### Study characteristics

Of the 12 eligible studies, one was a prospective cluster randomized controlled trial (25) and 11 were observational studies of a variety of designs, including cohort studies (14,16,19,22,23), programme descriptions (15,18,20,21,24) and a pilot study (17). Eight of the studies took place in the USA (14–16,18,19,21,23,25), one in Canada (24), one in New Zealand (17), and two in Europe (Spain (20) and Norway (22)).

### Study participants, interventions and outcomes

The level of detail provided on study participants varied and included general practitioners, primary care providers, family practice residents, urgent care clinics and community clinics. Four studies provided insufficient detail to clearly define participants (Table 1 and Supplementary Table S3) (15,18,20,21).

The interventions were wide-ranging and heterogeneous. Five studies disseminated syndromic data to clinicians (17,18,21,23–25), two disseminated microbiological data (14,19) and five disseminated a mixture of microbiological and syndromic data (15,16,20,22) (Table 1 and Supplementary Table S3). The majority of studies disseminated infection surveillance information via websites, electronic databases and emails. One study disseminated information through biweekly faxes (14), one via a tool embedded in the electronic health record to be available on demand (25) and one study allowed users

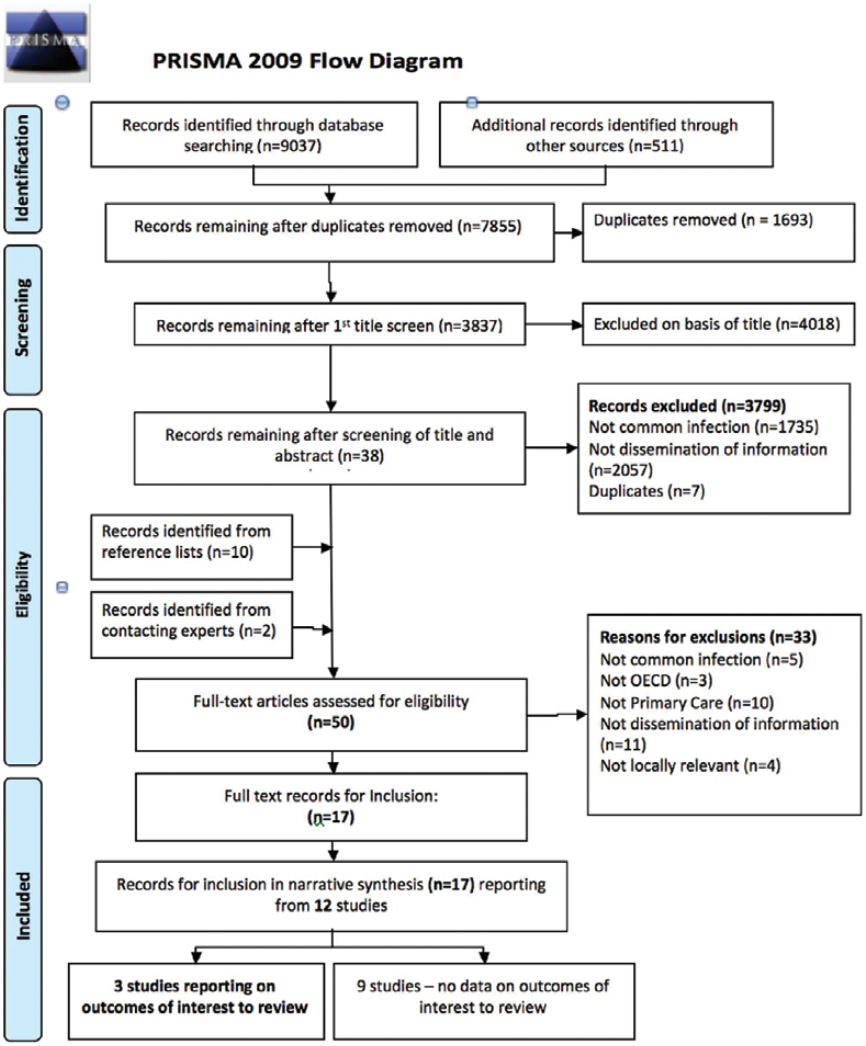


**Figure 1.** Systematic review flow chart (9). Infection surveillance in primary care. Years covered by review 1946–2016.

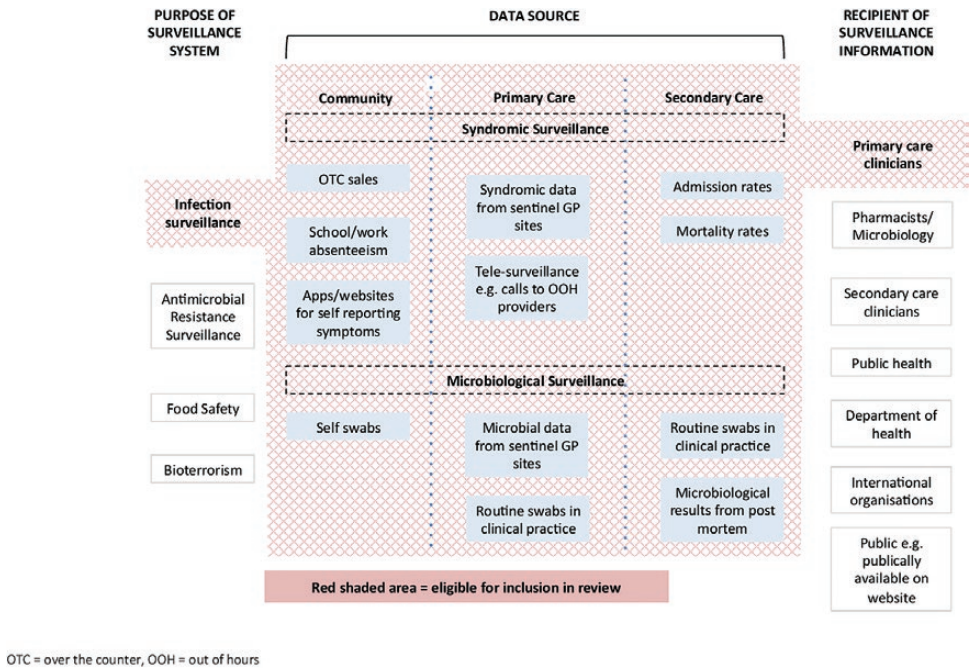


**Figure 2.** Schema of surveillance systems by purpose, data source and intended recipient. Infection surveillance in primary care. Years covered by review 1946–2016. OTC, over-the-counter; OOH, out-of-hours.

to define how they wanted to receive the data from a range of options (18) (Table 1 and Supplementary Table S3). The majority of the studies provided information on a daily or weekly basis (Table 1 and Supplementary Table S3). The studies included in this review presented the use of surveillance information for a range of different types of infections, including respiratory, gastrointestinal and skin infections (Table 1 and Supplementary Table S3). None of the studies described the use of a behavioural change model to design or implement their intervention.

A comparison group was described by three studies (14,23,25), and one additional study defined their planned comparison group (22) (Table 1 and Supplementary Table S3).

Three studies reported on antibacterial prescribing rates (14,23,25) (primary outcome), and two studies reported on antiviral prescribing rates (23,25) (secondary outcome; Table 2). The three studies reporting on outcomes of interest to this review all focussed on respiratory infections (14,23,25). No outcomes were reported on secondary care referral rates, harms, consultation rates, costs or diagnostic certainty (Supplementary Table S4).

### Antibacterial prescribing rates (Table 2)

The three studies that reported on antibacterial prescribing rates varied in the study design and included a cohort study with a historical control group (14), a retrospective cohort study (23) and a prospective cluster randomized controlled trial (25).

A reduction in antibacterial prescribing was seen following a 3-year educational and surveillance programme delivered by Temte *et al.* (14) to family practice residents with prescribing falling from 26.4% to 8.6% ($P = 0.01$) for upper respiratory infections. A reduction in antibacterial prescribing was reported by Hebert *et al.* (23) during a pandemic influenza period when compared with seasonal influenza periods: [odds ratio (OR) 0.72 (95% CI, 0.68 to 0.77), $P < 0.001$]. They also demonstrated that the likelihood of prescribing an antibacterial decreased as the number of febrile respiratory illness (FRI) cases that a physician had seen in the previous week increased—if 12+ patients were seen in the preceding week compared with 0–1 patients, antibacterial prescribing reduced [OR 0.57 (95% CI, 0.51 to 0.63), $P < 0.001$] (23). Shah *et al.* (25) reported a reduction in antibacterial prescribing following the introduction of an intervention providing clinicians with a syndromic heat map of influenza activity—they measured an absolute reduction in antibacterial prescribing of 5.1% during a period of moderate influenza activity ($P < 0.05$).

### Antiviral prescribing rates (Table 2)

Hebert *et al.* (23) described an increase in antiviral prescribing rates during a pandemic influenza period when compared with seasonal influenza periods: [OR 6.43 (95% CI, 5.02 to 8.25), $P < 0.001$). They also demonstrated that the likelihood of prescribing an antiviral agent increased as the number of FRI cases that a physician had seen in the previous week increased—if 12+ patients were seen in the preceding week compared with 0–1 patients, antiviral prescribing increased [OR 4.25 (95% CI, 3.42 to 5.28) $P < 0.001$) (23). Shah *et al.* (25) reported an absolute 1.6% increase in antiviral prescriptions for influenza-like illness (ILI) visits during a high ILI activity ($P$-value not <0.05 but actual numerical value not reported).

## Data synthesis and quality assessment

Further quantitative synthesis was not possible due to lack of numerical outcomes reported and high levels of heterogeneity between the studies. Due to the challenges of implementing complex interventions in a wide variety of clinical settings, there were numerous methodological challenges leaving studies open to relatively high levels of risk of bias (Tables 3 and 4).

# Discussion

## Summary of main findings

This review demonstrates the wide variety of surveillance systems and data sources that could support primary care antimicrobial

**Table 1.** Study characteristics of studies reporting on primary or secondary outcomes of interest. Infection surveillance in primary care. Years covered by review 1946–2016

| Author and year of publication | Country | Design | Participants | Intervention | | | Comparison |
|---|---|---|---|---|---|---|---|
| | | | Recipients of intervention | Intervention details | Microbiological (M) or syndromic (S) | Mode and frequency | |
| Temte (14), 1999 | USA | Cohort with historical control | Family practice residents starting in 1992 for 3 years ($n$ = 14) | Educational and surveillance program delivered over 3 years. Summary report of compiled results of viral cultures and other clinical specimens sent to eight different surveillance sites. Information provided a report specific to the site as well as regional, state and national trends | M: Respiratory viral culture results (respiratory). | Biweekly fax | Family practice residents' pre-intervention ($n$ = 8) |
| Hebert (23), 2012 | USA | Retrospective cohort | 69 physicians in 26 practices. Exposed group—7789 patient visits during the pandemic period versus 20 512 visits during the non-pandemic period | Study to examine the association between contextual factors and antimicrobial prescribing for a FRI. Effect of pandemic period—heavy media coverage, public anxiety, regular updates to physicians on management guidelines, epidemiological data and vaccine information | S: FRI | Alerts and information received during a pandemic period | Seasonal (non-pandemic) period used as control |
| Shah (25), 2014 (Supporting material (29)) | USA | Prospective cluster RCT | 27 GP practices (cluster randomized) | Syndromic heat map generated from data collected daily from EHRs to provide GPs with a point of care clinical decision support tool available via the EHR to GPs that generates a syndromic heat map for ILI, pertussis, GAS and paediatric asthma | M and S: ILI, pertussis, GAS and paediatric asthma | On demand via the electronic health record | 27 GP practices (cluster randomized) |

GAS, Group A Streptococcus; ILI, influenza-like illness; EHR, electronic health records.

**Table 2.** Planned or reported primary or secondary outcomes of interest to the review. Infection surveillance in primary care. Years covered by review 1946–2016

| Study | Primary outcomes | | | | | Secondary outcomes | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Antibiotic prescribing rates | | | | SCR H | Antimicrobial types | CR | Cost | DC |
| Temte (14), 1999 | A confidential review of randomly selected medical records to estimate the rates of antibiotic prescribing for upper respiratory infection (URI) and bronchitis for each resident in 1996 ($n$ = 14) and 1992 ($n$ = 8). Comparisons were made between 1992 and 1996 for the mean rates of antibiotic prescribing for URI and bronchitis among the charts reviewed using ANOVA | | | | | | | | |
| | | Mean antibiotic prescribing rate (absolute) | | | | | | | |
| | | Intervention group ($n$ = 14) | Control group ($n$ = 8) | | | | | | |
| | URI | 8.6% | 26.4% | $P$ = 0.01 | | | | | |
| | Bronchitis | 80.2% | 93.1% | NS | | | | | |
| | Composite | 28.8% | 52.3% | $P$ = 0.005 | | | | | |
| Hebert (23), 2012 | Of the 28 301 patient encounters for FRI with 69 physicians in 26 practices, an antibiotic was prescribed in 12 795 (45.2%) cases. Prescribing among physicians varied from 17.9% to 83.7%. Antibiotics were prescribed in 47.5% (9741 out of 20 512) of encounters during the seasonal period and 39.2% (3054 of 7789) during the pandemic period [OR 0.72 (95% CI, 0.68 to 0.77), $P$ < 0.001]. The likelihood of prescribing an antibiotic decreased as the number of FRI cases that a physician had seen in the previous week increased | | | | | Antivirals prescribed in 5.5% cases in seasonal periods and 12.6% during the pandemic period [OR 6.43 (95% CI, 5.02 to 8.25), $P$ < 0.001]. If physician had seen >12 patients with FRI in the preceding week, the odds of prescribing antivirals were 4.25 (95% CI, 3.42 to 5.28) compared with seeing 0–1 patients, $P$ < 0.001 | | | |
| | FRI cases seen in preceding week | OR | 95% Confidence interval | | | | | | |
| | 2–3 | 0.93 | 0.86 to 1.01 | | | | | | |
| | 4–6 | 0.84 | 0.77 to 0.91 | | | | | | |
| | 7–11 | 0.71 | 0.64 to 0.78 | | | | | | |
| | 12+ | 0.57 | 0.51 to 0.63 ($P$ < 0.001) | | | | | | |
| | Results compared with reference range of 0–1 patients. | | | | | | | | |
| Shah (25), 2014 (Supporting material (29)) | ILI visits: The intervention arm did not prescribe fewer antibiotics for ILI visits than the control arm overall (41.1% versus 41.3% $P$ = 0.90). High ILI activity—intervention group experienced absolute 2.0% reduction in antibiotic prescription for ILI visit (NS). Medium ILI activity—intervention group experienced absolute 5.1% reduction in antibiotic prescription for ILI visit ($P$ <0.05).All clinic visits: High ILI activity—absolute 1.0% reduction in antibiotic prescription ($P$ < 0.05). Medium ILI activity—absolute 1.7% reduction in antibiotic prescription ($P$ < 0.05) | | | | | Antiviral prescribingHigh ILI activity—intervention group experienced absolute 1.6% increase in antiviral prescription for ILI visit (NS).Medium ILI activity—intervention group experienced absolute 0.33% reduction in antiviral prescription for ILI visit ($P$ < 0.05).GAS specific antibioticsHigh GAS—intervention group absolute 3.3% increase*.Medium GAS—intervention group absolute 8.4% decrease*.Low GAS—intervention group absolute 6.7% decrease* | | | |

SCR, secondary care referral rates; H, Harms; CR, consultation rates (any measure of consultations); DC, diagnostic certainty; FRI, febrile respiratory illness; ILI, influenza-like illness; GAS, group A Streptococcus; URI = upper respiratory infection; NS, not significant; grey shaded, not reported. *Results significant at P < 0.05 value.

decision-making. We found few had been evaluated, but those that had shown promising, albeit methodologically weak, evidence that providing locally relevant, real-time epidemiological information improved antimicrobial prescribing in primary care.

## Strengths and limitations

We conducted a novel, rigorous, comprehensive review for evidence to support one potential solution to an internationally recognized public health problem. The small number of included studies prevented us from assessing the effects of publication bias (no studies were identified reporting an increase in antibacterial prescribing). Although the review set out to consider surveillance of any common infection relevant to primary care, the three studies included that reported on outcomes of interest to this review (14,23,25) focussed primarily on respiratory infections. It is important to recognize this limitation of the review and to take this into account when considering surveillance of non-respiratory infections. Even within respiratory infections, due to the low number of studies eligible for inclusion in the review, there are likely to be differences in application of surveillance data for different types of respiratory infection. For example, for influenza, outcomes from the use of surveillance information as a clinical decision support tool may vary depending on whether the clinician is in a locality experiencing expected seasonal activity of the virus, an epidemic or a pandemic.

## Results in context with other studies

Most existing surveillance literature focuses on two elements: first, how to optimize accurate, timely data (microbiological, syndromic, absenteeism, over-the-counter sales) completion (31–33) and second, distributing analyzed surveillance data to health departments and public health officials for outbreak detection and health service preparedness. As we have demonstrated, surveillance data are rarely targeted towards primary care clinicians with a view to changing clinical management. Qualitative research suggests that GPs are not

**Table 3.** Quality assessment for non-randomized intervention studies using ROBINS-I tool (13). Infection surveillance in primary care. Years covered by review 1946–2016

| Study | Bias due to confounding? | Bias in selection of participants into the study? | Bias in classification of interventions? | Bias due to deviation from intended interventions? | Bias due to missing data? | Bias in measurement of outcomes? | Bias in selection of the reported results? | Overall bias |
|---|---|---|---|---|---|---|---|---|
| Temte (14), 1999 | S | S | S | NI | S | S | M | S |
| Zelicoff (15), 2001 | NI | NI | NI | NI | NI | NI | NI | NI |
| Hammond (16), 2002 | C | S | S | S | NI | S | NI | C |
| Jones (17), 2004 | S | S | S | NI | NI | NI | NI | S |
| Daniel (18), 2005 | NI | NI | NI | NI | NI | NI | NI | NI |
| Gesteland (19), 2007 | S | S | S | S | S | S | NI | S |
| Gonzalez-Moran (20), 2008 | NI | NI | NI | NI | NI | NI | NI | NI |
| Olson (21), 2011 (Supporting material (28,30)) | NI | NI | NI | NI | NI | NI | NI | NI |
| Simonsen (22), 2011 (Supporting material (26,27)) | NI | NI | NI | NI | NI | NI | NI | NI |
| Hebert (23), 2012 | S | S | S | NI | M | NI | S | S |
| Price (24), 2014 | S | S | NI | NI | NI | NI | NI | S |

**Table 4.** Quality assessment for randomized intervention studies using Cochrane Risk Of Bias tool 2.0 (12). Infection surveillance in primary care. Years covered by review 1946–2016

| Study | Bias arising from the randomization process? | Bias due to deviations from intended interventions? | Bias due to missing outcome data? | Bias in measurement of outcomes? | Bias in selection of the reported results? | Overall bias |
|---|---|---|---|---|---|---|
| Shah (25), 2014 (Supporting material (29)) | SC | HR | SC | LR | HR | HR |

| KEY | | | | |
|---|---|---|---|---|
| M | Moderate risk of bias. | LR | Low risk of bias. |
| S | Serious risk of bias. | SC | Some concern. |
| C | Critical risk of bias. | HR | High risk of bias. |
| NI | No Information. | | |

even aware of what surveillance data is publically available and do not currently access this type of information in their clinical practice to support their diagnostic reasoning (34).

### Clinical and research implications

Even though only a small number of studies have demonstrated a trend towards reduced antibacterial prescribing with increased access to surveillance data for primary care clinicians, the evidence is not yet sufficiently mature to be used in routine practice, and significant investment would be required to make existing data sources ready for intervention. That said, even small improvements in the primary care use of antibacterials could have significant implications for reducing AMR (3,4) and patient demand for primary care consultations (35). To maximize the potential benefits of this type of intervention, future research needs to, first, establish what information, and using which delivery method, would be most valued by clinicians and to, second, assess effects using adequately powered, randomized studies of interventions underpinned by robust behaviour change methods.

## Conclusions

There is promising evidence that syndromic and microbiological epidemiological data can influence the use of antibacterials in primary care. Future research should use behaviourally informed interventions, tested using prospective randomized designs; and establish the mechanisms of behaviour change.

## Supplementary material

Supplementary data is available at *Family Practice* online.

## Declaration

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## References

1. WHO. Worldwide country situation analysis: response to antimicrobial resistance. 2015. http://www.who.int/drugresistance/documents/situationanalysis/en/. (accessed May/June 2017).
2. ESPAUR. *English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)*. Waterloo Road, London: Public Health England, 2016; pp. 1–181.
3. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010; 340: c2096.
4. Bryce A, Hay AD, Lane IF, *et al*. Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: systematic review and meta-analysis. *BMJ* 2016; 352: i939.
5. NICE. *Respiratory tract infections (self-limiting): prescribing antibiotics*. Piccadilly Plaza, Manchester: National Institute for Health and Clinical Excellence, 2008; pp. 1–20.
6. Cabral C, Lucas PJ, Ingram J, Hay AD, Horwood J. "It's safer to …" parent consulting and clinician antibiotic prescribing decisions for children with respiratory tract infections: an analysis across four qualitative studies. *Soc Sci Med* 2015; 136–137: 156–64.
7. Lucas PJ, Cabral C, Hay AD, Horwood J. A systematic review of parent and clinician views and perceptions that influence prescribing decisions in relation to acute childhood infections in primary care. *Scand J Prim Health Care* 2015; 33: 11–20.
8. Horwood J, Cabral C, Hay AD, Ingram J. Primary care clinician antibiotic prescribing decisions in consultations for children with RTIs: a qualitative interview study. *Br J Gen Pract* 2016; 66: e207–13.
9. Moher D, Shamseer L, Clarke M *et al*.; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4: 1.
10. OECD. Organisation for economic co-operation and development. 2016. http://www.oecd.org/ (accessed on 8 May 2017).
11. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. *Fam Med* 2005; 37: 360–3.
12. Higgins JPT, Stern JAC, Savović J *et al*. A revised tool for assessing risk of bias in randomized trials. In: Chandler J, McKenzie J, Boutron I, Welch V (eds). *Cochrane methods 2016*. 2016, vol. 10(Suppl 1), pp. 1–78. doi:10.1002/14651858.CD201601.
13. Sterne JA, Hernán MA, Reeves BC *et al*. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016; 355: i4919.
14. Temte JL, Shult PA, Kirk CJ, Amspaugh J. Effects of viral respiratory disease education and surveillance on antibiotic prescribing. *Fam Med* 1999; 31: 101–6.
15. Zelicoff Al, Brillman J, Forslund DW *et al*. The Rapid Syndrome Validation Project (RSVP). *Proc AMIA Symp* 2001; 771–5.
16. Hammond L, Papadopoulos S, Johnson CF *et al*. Use of an internet-based community surveillance network to predict seasonal communicable disease morbidity. *Pediatrics* 2002; 109: 414–8.
17. Jones NF, Marshall R. Evaluation of an electronic general-practitioner-based syndromic surveillance system—Auckland, New Zealand, 2000–2001. *MMWR Suppl* 2004; 53: 173–8.
18. Daniel JB, Heisey-Grove D, Gadam P *et al*. Connecting health departments and providers: syndromic surveillance's last mile. *MMWR Suppl* 2005; 54: 147–50.
19. Gesteland PH, Samore MH, Pavia AT *et al*. Informing the front line about common respiratory viral epidemics. *AMIA Annu Symp Proc* 2007; 2007: 274–8.
20. Gonzalez Moran F, Munoz Criago I, Vanaclocha H. Real time information. A necessary tool in epidemiological surveillance. *Gra Sanit* 2008; 22: 162–7.
21. Olson DR, Paladini M, Lober WB, Buckeridge DL; ISDS Distribute Working Group. Applying a new model for sharing population health data to National Syndromic Influenza Surveillance: DiSTRIBuTE project proof of concept 2006 to 2009. *PLoS Curr* 2011; 3: RRN1251–13.
22. Simonsen GS, Chomutare T, Ilebrekke L *et al*. Real-time local epidemiological data through the internet as a management tool for infections in the community [Abstract P1306]. 21st European Congress of Clinical Microbiology and Infectious Diseases, Milan, Italy, May 7–10, 2011.
23. Hebert C, Beaumont J, Schwartz G, Robicsek A. The influence of context on antimicrobial prescribing for febrile respiratory illness: a cohort study. *Ann Intern Med* 2012; 157: 160–9.
24. Price D, Chan D, Greaves N. Physician surveillance of influenza: collaboration between primary care and public health. *Can Fam Phys* 2014; 60: e7–15.
25. Shah N, Ridgway JP, Konchak C *et al*. What's going around? A prospective cluster randomized trial to evaluate a novel, real-time, syndromic surveillance tool's effect on clinical decision making amongst primary care providers. *Open Forum Infect Dis* 2014; 1(Suppl 1): S78.
26. Bellika JG, Sue H, Bird L *et al*. Properties of a federated epidemiology query system. *Int J Med Inform* 2007; 76: 664–76.
27. Bellika JG. *Snow Disease Surveillance Systems Study (Snow)*. Tromso, 2010. https://clinicaltrials.gov/ct2/show/NCT01232686. (accessed May/June 2017).
28. Reeder B, Revere D, Olson DR, Lober WB. Perceived usefulness of a distributed community-based syndromic surveillance system: a pilot qualitative evaluation study. *BMC Res Notes* 2011; 4: 187.

29. Robiscek A. How does the clinical tool 'What's going around' affect clinical practice (WGA). 2013. https://clinicaltrials.gov/ct2/show/NCT01979588. (accessed May/June 2017).
30. Lober WB, Reeder B, Painter I *et al*. Technical description of the distribute project: a community-based syndromic surveillance system implementation. *Online J Public Health Inform* 2014; 5: 224.
31. Choi J, Cho Y, Shim E, Woo H. Web-based infectious disease surveillance systems and public health perspectives: a systematic review. *BMC Public Health* 2016; 16: 1238.
32. Velasco E, Agheneza T, Denecke K, Kirchner G, Eckmanns T. Social media and internet-based data in global systems for public health surveillance: a systematic review. *Milbank Q* 2014; 92: 7–33.

33. Milinovich GJ, Williams GM, Clements AC, Hu W. Internet-based surveillance systems for monitoring emerging infectious diseases. *Lancet Infect Dis* 2014; 14: 160–8.
34. Anderson EC, Lane I, Kesten JM *et al*. Real-time paediatric respiratory tract infection (RTI) community surveillance: a qualitative interview study of clinicians? Perspectives on the use, design and potential impact of a planned intervention. *Front Public Health* 2017. doi:10.3389/conf.FPUBH.2017.03.00020.
35. Ashworth M, Charlton J, Ballard K, Latinovic R, Gulliford M. Variations in antibiotic prescribing and consultation rates for acute respiratory infection in UK general practices 1995–2000. *Br J Gen Pract* 2005; 55: 603–8.